

Remarks

Claims 1-4, 6-10, 12-15, 17-22, 24 and 25 are pending in the application. Claims 17-18, and 25 have been withdrawn from consideration due to the Examiner's previous restriction requirement. Claims 5, 11, 16 and 23 had been canceled in a previous reply. Applicants reserve the right to file divisional and continuing applications directed to the subject matter of any claim withdrawn, cancelled or amended for any reason. Applicants do not acquiesce to the propriety of any of the Examiner's prior rejections and does not disclaim any subject matter to which Applicants are entitled. *Cf. Warner Jenkinson Co. v. Hilton-Davis Chem. Co.*, 41 USPQ.2d 1865 (US 1997).

Moreover, Applicants also do not acquiesce to the accuracy or propriety of the Examiner's characterization and review of Applicant's remarks at pages on pages 14-18 of the Final Office Action mailed May 26, 2009 ("OA"). The Examiner continues to fail to establish a *prima facie* case of obviousness of the subject claims for the reasons stated in Applicants' Reply Under 37 C.F.R. § 1.116 dated July 17, 2008, and Reply & Amendment Under 37 C.F.R. § 1.111 dated December 29, 2008, which are hereby incorporated by reference, and for the following additional reasons.

I. Claim Objections

Applicants have submitted proposed amendments to claims 1 and 24 to correct the informalities identified by the Examiner on page 3 of the OA.. Applicants have also proposed an amendment to claim 19 to correct an obvious grammatical error. Entry of these proposed amendments is respectfully requested and in view of these proposed amendments, Applicants respectfully request that the objections to claims 1 and 24 be withdrawn

II Rejections under 35 U.S.C. § 103

To maintain a proper rejection under 35 U.S.C. § 103, the Examiner must meet four conditions to establish a *prima facie* case of obviousness. First, the Examiner must show that the prior art suggested to those of ordinary skill in the art that they should make the claimed composition or device or carry out the claimed process. Second, the Examiner must show that the prior art would have provided one of ordinary skill in the art with a reasonable expectation of success. Both the suggestion and the reasonable

expectation of success must be adequately founded in the prior art and not in an applicant's disclosure. Third, the prior art must teach or suggest all the claim limitations. *In re Vaeck*, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991). Fourth, if an obviousness rejection is based on some combination of prior art references, the Examiner must show a suggestion, teaching, or motivation to combine the prior art references ("the TSM test"). *In re Dembiczak*, 50 U.S.P.Q.2d 1614, 1617 (Fed. Cir. 1999). Following *KSR Int'l Co. v. Teleflex, Inc.*, this fourth prong of the *prima facie* obviousness analysis must not be applied in a rigid or formulaic way such that it becomes inconsistent with the more flexible approach of *Graham v. John Deere*, 383 U.S. 1, 17-18 (1966). 550 U.S. 398 (2007); 127 S. Ct. 1727 (2007). It must still be applied, however, as the TSM test captures the important insight that "a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." *Id.* citing *United States v. Adams*, 383 U.S. 39, 50-52 (1966).

A. *Sheriff in View of Herzog – Claims 1, 3-4, 6-7, 9-10, 12, and 14- 15*

Claims 1, 3-4, 6-7, 9-10, 12, and 14-15 stand rejected under 35 U.S.C. § 103 as allegedly obvious over Sheriff et al., Reg. Pept. 75-76: 309-318, 1998 ("Sheriff") in view of Herzog et al., PNAS 89: 5794-5798, 1992 ("Herzog"). Applicants respectfully traverse for the reasons set forth below.

1. *Range of Concentration*

The Examiner states that Sheriff teaches

a method to determine the neuropeptide Y or NPY induced effect on CREB pathway function, such as CREB phosphorylation and CaM kinase activity. Sheriff et al. specifically teach the transfection of cells from the neuroblastoma cell line SK-N-BE2 with a fusion gene containing the CRE site linked to firefly luciferase (indicator) gene. The reference further teaches that the treatment of the transfected cells with NPY and forskolin results in a significant increase of luciferase activity as compared to control cells treated with forskolin but not with the NPY (Abstract; Results: Section 3.5; Figure 5, 5th and 6th bar). Furthermore, Sheriff et al. demonstrate that the luciferase activity in control cells treated with NPY but not with forskolin is not significantly different from the activity elicited by control cells that are not treated with either forskolin or with NPY (Figure 5, 1st and 2nd bar). Sheriff et al further teach that NPY exerts several biological and cognitive functions (e.g. modulation of memory,

inhibition of anxiogenic activity, feeding behavior, etc.), by activating the CREB pathway.

OA at page 5. The Examiner admits, however, that Sheriff does not teach "repeating the method steps with a range of concentrations of the compound or NPY."

The Examiner asserts that "since the disclosures does not specify criticality of the claimed range of doses, optimization within prior art conditions or through routine experimentation is obvious to one skilled in the art." The Examiner then cites to MPEP 2144.05 in support of this statement.

Applicants respectfully traverse for the reasons stated in their Reply Under 37 C.F.R. § 1.116 dated July 17, 2008, and Reply & Amendment Under 37 C.F.R. § 1.111 dated December 29, 2008, which are hereby incorporated by reference, and for the following additional reasons. As the Supreme Court has noted, "[e]ach element contained in a patent claim is deemed material to defining the scope of the patented invention." *Warner Jenkinson Co. v. Hilton-Davis Chem. Co.*, 41 U.S.P.Q.2d 1865 (US 1997). In making the conclusion that the element "repeating steps a) to d) with a range of different concentrations of said test compound selected in step d)" is not "critical," the Examiner is reading this element out of the claim. This is impermissible – it is black letter law that an Examiner must show that each element is disclosed by the prior art to establish a *prima facie* case of obviousness. See, e.g., *In re Royka*, 490 F.2d 981 (CCPA 1974), and *In re Vaeck*, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991).

Furthermore, the MPEP section cited by the Examiner is inapposite. The Applicants are not claiming the "optimum or workable ranges" of a compound, nor are they distinguishing their claims from a prior art reference by pointing out differences in concentration of a compound, the situation to which MPEP 2144.05 applies. Instead, the element "repeating steps a) to d) with a range of different concentrations of said test compound selected in step d)" focuses on exactly that – repeating the steps of the claimed method with a range of different concentrations of the test compound selected in a separate step.

2. *Gene Expression*

The Examiner asserts that

Sheriff et al. also teach contacting cells (not transfected) of the neuroblastoma cell line with NPY and forskolin, and assess the expression of endogenous gene

containing CRE (Y1 receptor). The reference further teaches that although NPY treatment increases the Y1 mRNA expression, forskolin is more potent in upregulating Y1 receptor message, when compared to untreated controls (page 314, Section 3.6 of Results; Figure 6).

OA at page 7. The Examiner admits that Sheriff does not teach "the addition of both NPY and forskolin to neuroblastoma cells for the analysis of gene expression," but reasons that "in the absence of unexpected results, it would have been *prima facie* obvious to one of ordinary skill in the art to combine the teachings of the reference and to treat the cells with both NPY (as the candidate compound) and forskolin." *Id.* The examiner cites *In re Kerkhoven*, 626 F.2d 846, 205 USPQ 1069 (CCPA 1980) in support of this obviousness rejection.

Applicants respectfully traverse for the reasons stated in their Reply Under 37 C.F.R. § 1.116 dated July 17, 2008, and Reply & Amendment Under 37 C.F.R. § 1.111 dated December 29, 2008, which are hereby incorporated by reference, and for the following additional reasons. *In re Kerkhoven* is inapposite because it relates to a different type of claim. The claim at issue in *In re Kerkhoven* recited a process of creating a composition of matter, whereas Applicants claim methods comprising screening a plurality of compounds. Furthermore, in referencing the "absence of unexpected results," the Examiner improperly shifts to Applicants the burden of *disproving* obviousness before the Examiner has made the required *prima facie* case of obviousness.

3. *Hippocampal Neurons*

The Examiner admits that Sheriff does not teach "contacting cells that are hippocampal neurons" or "screening a plurality of compounds." The Examiner argues that, "as in the case of neuroblastoma, the hippocampus comprise cells of neural origin comprising neurons and *absent evidence to the contrary*, contacting of NPY [*sic*] and forskolin to upregulate Y1 gene expression in hippocampal neurons would be obvious to one skilled in the art in view of Sheriff et al, and Herzog et al." (emphasis added).

Applicants respectfully traverse for the reasons stated in their Reply Under 37 C.F.R. § 1.116 dated July 17, 2008, and Reply & Amendment Under 37 C.F.R. § 1.111 dated December 29, 2008, which are hereby incorporated by reference, and for the following additional reasons. As stated above, in stating "absent evidence to the

contrary," the Examiner improperly shifts to Applicants the burden of *disproving* obviousness before the Examiner has made the required *prima facie* case of obviousness. The Examiner fails to set forth any evidence that the prior art teaches or suggests contacting hippocampal neurons with NPY and forskolin. The Examiner also fails to provide any evidence that the prior art, including Sheriff and Herzog, teaches or suggests "screening a plurality of compounds."

In view of the arguments set forth above, Applicants respectfully request that the Examiner reconsider and withdraw the pending rejections of claims 1, 3-4, 6-7, 9-10, 12, and 14-15 under 35 U.S.C. § 103.

B. *Sheriff in View of Herzog and in further view of Barad – Claims 19(a-k), 20-22, and 24*

Claims 19(a-k), 20-22, and 24 stand rejected under 35 U.S.C. § 103 as allegedly obvious over Sheriff in view of Herzog and in further view of Barad et al., PNAS 95: 15020-15025, 1998 ("Barad").

Applicants respectfully traverse for the reasons stated in their Reply Under 37 C.F.R. § 1.116 dated July 17, 2008, and Reply & Amendment Under 37 C.F.R. § 1.111 dated December 29, 2008, which are hereby incorporated by reference, and for the following additional reasons. Applicants also incorporate their arguments above and note that neither Sheriff nor Herzog teaches or suggests screening a plurality of compounds to determine the ability of the compounds to enhance the cyclic adenosine monophosphate (cAMP) response element binding protein (CREB) pathway and identifying the compounds as a candidate cognitive enhancer compound based on the selection parameters of the pending claims. Barad does not remedy these deficiencies of Sheriff and Herzog.

Moreover, the Examiner fails to set forth any evidence that the prior art teaches or suggests substituting hippocampal neurons for hippocampal slices other than the mere conclusory statement that "[t]he person of ordinary skill in the art would have been motivated" to do so. In addition, the Examiner must show that the prior art would have provided one of ordinary skill in the art with a reasonable expectation of success, and the similarly conclusory statement by the Examiner that "gene expression studies using individual neurons were well-established" again fails to meet the requisite

standard. Both the suggestion and the reasonable expectation of success must be adequately founded in the prior art and not in an applicant's disclosure – the Examiner's conclusory statements on page 12 have no basis in the cited prior art and the Examiner again improperly shifts to Applicants the burden of *disproving* obviousness before the Examiner has made the required *prima facie* case of obviousness.

Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the pending rejections of claims 19(a-k), 20-22, and 24 under 35 U.S.C. § 103 as allegedly obvious over Sheriff in view of Herzog and in further view of Barad.

C. *Sheriff in View of Herzog and in further view of Barad – Claims 2, 8 and 13*

Claims 2, 8 and 13 stand rejected under 35 U.S.C. § 103 as allegedly obvious over Sheriff in view of Herzog and in further view of Barad. The Examiner admits that Sheriff, Herzog, and Barad "do not teach that the cells are contacted with the compound before contacting the CREB stimulating agent," but improperly reasons that it "would have been . . . obvious to the person of ordinary skill in the art at the time the claimed invention was made to determine the sequential addition of compounds to be added to neuroblastoma cells or hippocampal cells for identifying compounds that enhance the CREB pathway function" because "the disclosure does not specify criticality of the claimed sequence of addition of the test/candidate compound and the CREB function stimulating agent."

Applicants respectfully traverse for the reasons stated in their Reply Under 37 C.F.R. § 1.116 dated July 17, 2008, and Reply & Amendment Under 37 C.F.R. § 1.111 dated December 29, 2008, which are hereby incorporated by reference, and for the following additional reasons. As the Supreme Court has noted, "[e]ach element contained in a patent claim is deemed material to defining the scope of the patented invention." *Warner Jenkinson Co. v. Hilton-Davis Chem. Co.*, 41 USPQ.2d 1865 (US 1997). In making the conclusion that the claimed element wherein "cells are contacted with said test compound prior to contact with said CREB function stimulating agent" is not "critical," the Examiner is improperly reading this element out of the claim to make this rejection. This is impermissible – it is black letter law that an Examiner must show that each element is disclosed by the prior art to establish a *prima facie* case of obviousness. *See, e.g., In re Royka*, 490 F.2d 981 (CCPA 1974), and *In re Vaeck*, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991).

Furthermore, Applicants note that neither Sheriff nor Herzog teaches or suggests screening a plurality of compounds to determine the ability of the compounds to enhance the cyclic adenosine monophosphate (cAMP) response element binding protein (CREB) pathway and identifying the compounds as a candidate cognitive enhancer compound based on the selection parameters of the pending claims. Barad does not remedy these deficiencies of Sheriff and Herzog.

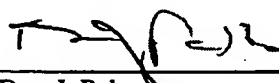
Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the pending rejections of claims 2, 8 and 13 under 35 U.S.C. § 103 as allegedly obvious over Sheriff in view of Herzog and in further view of Barad.

CONCLUSION

Applicants have properly and fully addressed each of the Examiner's grounds for rejection. Applicants submit that the present application is now in condition for allowance. If the Examiner has any questions or believes further discussion will aid examination and advance prosecution of the application, a telephone call to the undersigned is invited. If there are any additional fees due in connection with the filing of this amendment, please charge the fees to undersigned's Deposit Account No. 50-1067. If any extensions or fees are not accounted for, such extension is requested and the associated fee should be charged to our deposit account

Respectfully submitted,

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